REMARKS

In the instant Action, Claims 11 and 52-55 are listed as pending, Claims 11, 52 and 53 are listed as allowed, and Claims 54 and 55 are listed as rejected.

Applicants appreciatively note that the Examiner withdrew the restriction requirement, as set forth in the Office action mailed on 28 August 2003, as to Claims 54 and 55, directed to a method of treating a medical disorder involving the PTH2 receptor, since the claims require all the limitations of an allowable claim.

The Examiner has rejected Claims 54 and 55 under 35 U.S.C. §112, first paragraph, because the subject matter allegedly was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. Specifically, the Examiner alleged that "[t]he specification is not enabling for the limitations of the claims wherein a medical disorder is treated using the PTH2 analogue of SEQ ID NO: 16." (*See* page 3 of the instant Action)

At page 4 of the instant Action, the Examiner acknowledges that "[m]ost experimental peptides produced by the Applicants antagonized receptor binding of competing ligands with increased specificity (compared to PTH-receptor binding) as well as affinity (Specification, p. 22 and 23)." In view of this comment by the Examiner, Applicants have amended Claim 54 hereinabove such that Claim 54 is no longer directed to a method of treating a medical disorder. Claim 54, as amended, is directed to "[a] method of inhibiting the activation of the PTH2 receptor, which comprises contacting the PTH2 receptor with an analogue according to claim 52." As Claim 54 has been amended to be consistent with the Examiner's acknowledgement the allowed compounds of the present application are shown to antagonize receptor binding with increased specificity as well as affinity, Applicants respectfully submit that Claim 54, as amended, is allowable. Applicants request the reconsideration and withdrawal of the rejection of Claim 54 under 35 U.S.C. §112, first paragraph.

Likewise, Applicants have amended Claim 55 hereinabove such that Claim 55 is directed to a method of treating medical disorder that results from altered or excessive action of the PTH2 receptor wherein said medical disorder is limited only to abnormal CNS function and abnormal pancreatic functions. It should be noted that Applicants have deleted "divergence from normal

mineral metabolism and homeostasis, male infertility, abnormal blood pressure" and "hypothalamic disease", without waiver or prejudice, from Claim 55, to allay the Examiner's concern of "the breadth of the claims which embrace many unrelated diseases". (*See* page 5 of the instant Action)

The Examiner's first objection is that "no *in vivo* tests were performed and no patients or animals were administered the peptides." (*See* page 4 of the instant Action) However, there is no requirement under MPEP, 37 C.F.R., or 35 U.S.C, for *in vivo* tests to satisfy the enablement prong of 35 U.S.C. §112, first paragraph.

Next, the Examiner alleges that "there was no nexus established by the Disclosure as to the connection between the cellular data presented and the underlying mechanisms of these varied diseases." (*See* page 4 of the instant Action) As noted above, Claim 55 has been amended to be directed only to abnormal CNS function and abnormal pancreatic functions, and there is ample support in the specification of the present application to establish the requisite nexus. At page 1, lines 22-26 of WO 99/57139, which is the PCT publication number corresponding to the present application, it is stated that "The PTH2 receptor is localized predominantly in the brain and pancreas, in contrast to PTH/PTHrP receptor, which is primarily localized in bone and the kidney, the principal target tissue for PTH action." Further, at page 3, lines 18-23, of WO 99/57139, there is provide the following passage:

> Interestingly, PTH2 receptor mRNA is not detected in bone or osteosarcoma cell lines, but is expressed in a number of tissues including the exocrine pancreas, lung, heart, vasculature, and epididymis, and is most abundant in the brain (Usdin, T.B., et al., 1996, Endocrinology, 137:4285-4297).

Further, at page 4, lines 4-13, of WO 99/57139, there is provide the following passage:

> The physiological function of the PTH2 receptor because of its high abundance and distribution in the brain suggests that it may act as a neurotransmitter receptor. PTH has been found in the central nervous system (CNS) (Harvey, S., et al., 1993, J. Endocrinol. 139:353-361), therefore, it is possible that endogenous PTH2 receptor specific ligands, which are distinct from PTH, do exist in the CNS. Recently, Usdin reported the isolation of 'PTH2 receptor binding activity' from the hypothalamus which was immunologically distinct from PTH.

As such, even though it would have enabled a skilled artisan to use the allowed compounds of Claim 52 to treat all of the medical disorders that results from altered or excessive action of the

PTH receptor based on the knowledge in the prior art that the PTH receptor is found in the brain, pancreas, lung, heart, vasculature, epididymis, etc., Applicants have amended Claim 55 to be directed only to abnormal CNS function and abnormal pancreatic functions in view of the fact that the PTH2 receptor is localized predominantly in the brain and pancreas, and to place this application in a condition for allowance.

Next, the Examiner alleges that "[a]lthough it is difficult to prove a negative, it seems clear that the diseases mentioned above do not all involve the PTH2 receptor." (*See* page 4 of the instant Action) Initially, it should be noted that Claim 55, as amended, is limited to "[a] method of treating a medical disorder that results from altered or excessive action of the PTH2 receptor." As noted above, the PTH2 receptor is localized predominantly in the brain and pancreas; therefore, the burden is shifted to the Examiner to actually prove the negative that the claimed method of treating abnormal CNS or pancreatic functions that result from altered or excessive action of the PTH2 receptor, does not involve the PTH2 receptor.

Lastly, it is well established that 35 U.S.C. §112, first paragraph, requires only objective enablement for the claimed invention. Applicants submit that the teachings of the specification, and the cited prior art teachings, along with the *in vitro* experimental results, fully enable the skilled artisan to proceed with normal experimentation to practice the claimed method. Applicants further submit that, in the biological sciences, testing usually proceeds from *in vitro* testing in model systems to *in vivo* testing in model animals, eventually leading to *in vivo* testing in mammals such as humans. Skilled artisans routinely experience failure along with success and accept that retesting, reformulating and repetition of even successful experiments are all within the norm for biological testing.

In view of the foregoing, Applicants respectfully submit that Claims 54 and 55, as amended, are allowable. Applicants request the reconsideration and withdrawal of the rejection of Claims 54 and 55 under 35 U.S.C. §112, first paragraph.

CONCLUSION

Reconsideration of the instant Action, entry of the requested amendments, and allowance of the all pending claims are respectfully requested.

Prompt and favorable action is solicited.

Examiner Wegert is invited to telephone Applicants' attorney at (508) 478-0144 to facilitate prosecution of this application.

With the exception of the fee for the aforementioned extension, Applicants are unaware of any additional fees due and owing with respect to this filing, however, if the Applicants' understanding is incorrect, the Commission is authorized to apply any charges and/or credits to Deposit Account No. 50-0590 referencing attorney docket number 073/US/PCT/US.

Respectfully submitted,

Date: 8/4/2008

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